Helium-3 ADC at Very Short Time Scales Using an SSFP-based Imaging Pulse Sequence

Karen E Mooney[1,2], John P. Mugler III[3], Talissa A. Altes[3], Gordon D. Cates, Jr. [2,3], Eduard E. de Lange[3], Jaime F. Mata[3], W. A. Tobias[2], and G. Wilson Miller[3]

[1]Radiation Oncology, University of Maryland SOM, Baltimore, MD, United States, [2]Physics, University of Virginia, Charlottesville, Virginia, United States, [3]Radiology, University of Virginia, Charlottesville, Virginia, United States

Introduction: The purpose of the present work is to map the helium-3 apparent diffusion coefficient (ADC) in human lungs at diffusion times much less than a millisecond. The motivation for measuring diffusivity over a short time duration in a restrictive environment such as the lung parenchyma is that short diffusion times correspond to short length scales, and thus may provide greater sensitivity to subtle alterations of alveolar structure in diseases such as emphysema. The main disadvantage to using short diffusion times to generate an ADC map is that there is a smaller difference between the diffusion-weighted and the non-diffusion-weighted signals, which increases the noise in the ADC measurement. To help increase the SNR of the ADC maps made at Δ=500μs, we employed a balanced SSFP pulse sequence which can provide up to 3-4 times the signal of a spoiled GRE pulse sequence when applied to hyperpolarized magnetization [1, 2]. A previous attempt to incorporate diffusion-sensitization into a balanced SSFP pulse sequence to measure helium-3 diffusivity delivered results that were extremely sensitive to magnetic field variations [3]. We have developed a method that is much more robust in the presence of off-resonance magnetization, in which diffusion-sensitization is incorporated into a balanced SSFP pulse sequence by placing a bipolar diffusion-sensitizing gradient in each TR window, either before or after the data acquisition period.

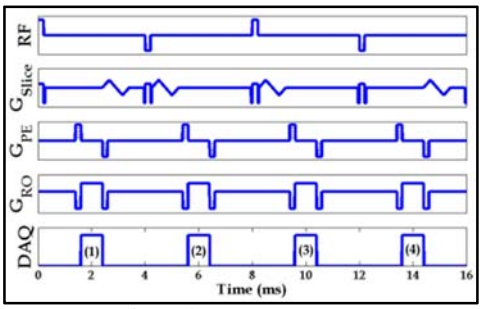

Figure 1: Before/After SSFP DWI pulse sequence. Four images are line-interleaved which alternate the diffusion gradients *after* DAQ (1 and 4), and diffusion gradients *before* DAQ (2 and 3).

Materials and Methods: Our SSFP DWI pulse sequence is illustrated in Figure 1. Four interleaved images are acquired, two with diffusion-sensitizing gradients applied *before* data acquisition, and two with the same gradients applied *after* the acquisition in the following order: (1) after, (2) before, (3) before, and (4) after. By acquiring the data at the same echo time (TE=TR/2) for all images, any T2* dependence cancels when ratios of the images are taken. By averaging images with similar diffusion sensitization but opposite RF phase and acquisition order, effects due to RF asymmetry and longitudinal relaxation also cancel. The ADC was calculated on a pixel by pixel basis from the four images as follows:

$\frac{S_{Before\,Avg}}{S_{After\,Avg}} = e^{-b*ADC}$, $ADC = -\frac{1}{b} * \ln\frac{S_2+S_3}{S_1+S_4}$, where b is the conventionally defined b-value of the bipolar diffusion-sensitizing gradient. We used this pulse sequence to measure the ADC of helium-3 in three human subjects: a healthy non-smoker, a long-term smoker, and a subject diagnosed with emphysematous COPD. The helium-3 was polarized to >50% using a hybrid rubidium-potassium SEOP polarizer [4]. The subjects inhaled 300*mL* of He-3 diluted with medical grade nitrogen (1150*mL*, 290*mL*, and 400*mL* respectively). Images were acquired using a 1.5T scanner (Siemens Avanto) using a rigid elliptical volume coil (Rapid Biomedical). Pulse sequence parameters included: TR=4.2*ms*, α=20°, *BW*=780*Hz/Px*, in-plane resolution of 6.6*mm x* 6.6*mm* zero-filled to 3.3*mm x* 3.3*mm*, 6-8 coronal slices with TH=20*mm*. The diffusion-sensitizing gradient consisted of a bipolar pair of triangular gradients with G_{max}=27*mT/m* and Δ=500*μs*, giving a b-value of b=0.1*s/cm*^{2}. ADC maps were calculated using the formula above, after applying a threshold mask of (0.1*Max. Signal). The mean ADC outside the major airways was calculated over each slice, by excluding pixels with ADC>0.8*cm*^{2}*/s*.

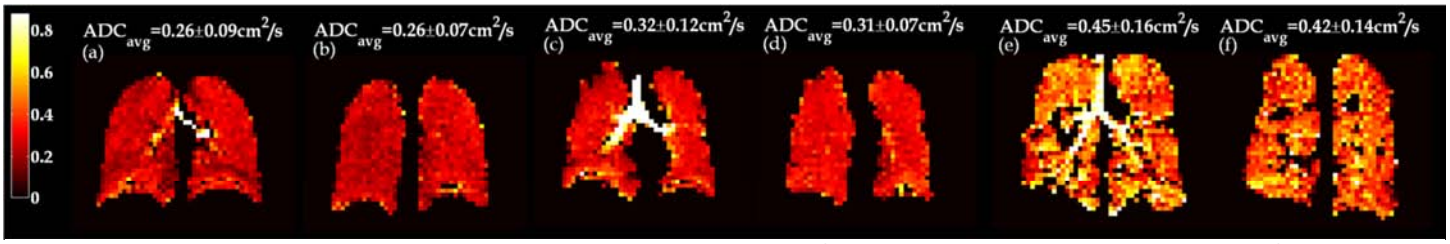

Figure 2: Helium-3 ADC maps with mean ADC (non-airway) and standard deviation of (a-b) a healthy volunteer, (c-d) a smoker, and (e-f) a subject with COPD. All three central slices show nearly free diffusion in the large airways *(ADC=0.8*~0.9*cm*^{2}*/s*). The diffusion coefficient measured in the bulk of the lung was higher in the subject with COPD (f) at *ADC*=0.42*cm*^{2}*/s* than in both the healthy subject at *ADC*=0.26*cm*^{2}*/s* (b) and the smoker at *ADC*=0.31*cm*^{2}*/s* (d).**

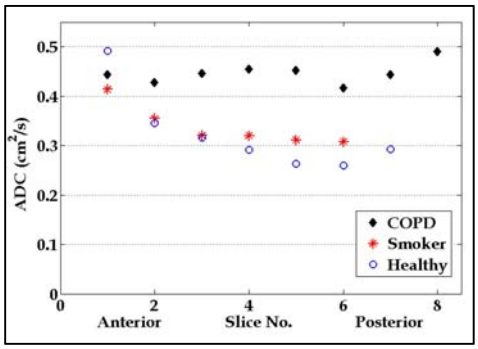

Figure 3: Mean ADC vs Slice Position. The central lung slices (shown in Fig. 2a, c, e) are slice 4 for the smoker and slice 5 for the healthy and the COPD subjects.

Results: Two slices from each subject are shown in Figure 2: a central lung slice which includes a portion of the trachea and main bronchi (a, c, and e), and a posterior slice which contains mostly parenchyma (b, d, and f). In all subjects, the diffusivity measured in the large airways represents nearly free diffusion, with *ADC* =0.8~0.9*cm*^{2}*/s*. In the healthy subject and the smoker (a-d), ADC values in the parenchyma are relatively low and uniform. In the COPD subject (e-f), ventilation was patchy which resulted in locations were no ADC was calculated, and ADC values in the parenchyma were higher and less uniform. Figure 3 shows the average ADC value over each coronal slice in all three subjects, excluding the large airways. In the most anterior slice, the ADC values measured in the healthy subject and the smoker were significantly larger than in the other slices. We are unsure whether this trend is real, or is an artifact of off-resonance or partial-volume effects.

Conclusion: We mapped the helium-3 ADC in human subjects at a diffusion time of Δ=500μs, the shortest duration over which this measurement has been reported, using an SSFP DWI pulse sequence developed for this purpose. The average value of helium-3 ADC measured in our healthy subject (0.26*cm*^{2}*/s*) is higher than typical ADC values (0.20*cm*^{2}*/s*) previously reported at diffusion times of Δ=1-2*ms*. This trend is expected, and is consistent with the gas being less restricted over the shorter measurement time. Now that basic sensitivity has been demonstrated, further optimization of this SSFP DWI method should include working to decrease TR to reduce susceptibility to banding artifacts near the diaphragm, and investigating the source of elevated ADC values in the anterior lung.

Acknowledgements: Supported by NIH grant R21 HL089525, and by Siemens Medical Solutions.

References: [1] Mugler JP 3rd et al. ISMRM 2002; 2019
[2] Wild JM et al. JMR 2006; 183:13-24
[3] Mooney K et al. ISMRM 2012; 1894
[4] Mooney K et al. ISMRM 2009; 2166